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Out-of-Hospital Cardiac Arrest: Pre-hospital Management

1. Marcus Eng Hock Ong MBBS, MPH

Department of Emergency Medicine, Singapore General Hospital, Singapore

Health Services and Systems Research, Duke-NUS Medical School, Singapore

2. Gavin D Perkins

Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Heart of England NHS Foundation Trust, Birmingham, UK

3. Alain Cariou

Medical Intensive Care Unit, AP-HP, Cochin Hospital, Paris, France

Paris Descartes University, Paris, France

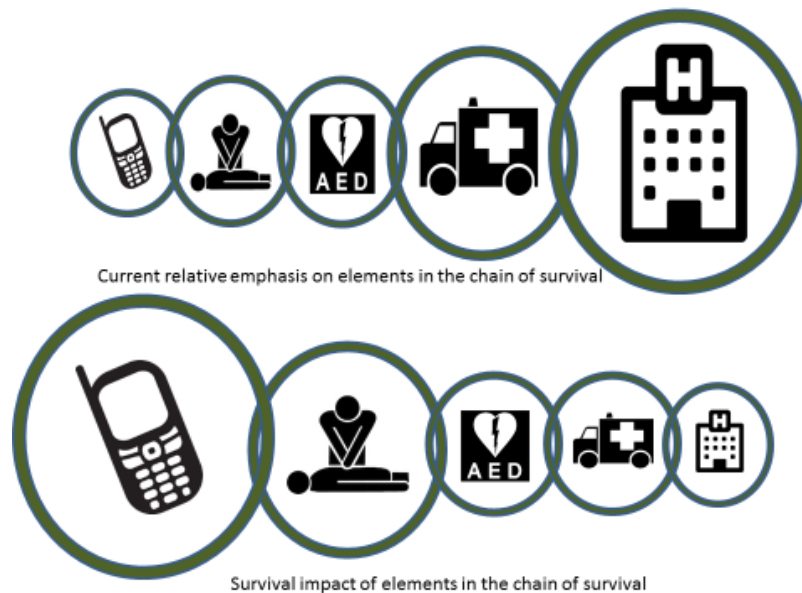
Abstract (no more than 150 words)

Sudden out of hospital cardiac arrest is the most time critical medical emergency. In this expert opinion and literature review, we consider important issues in the pre-hospital management of cardiac arrest. Successful resuscitation is reliant on a strong chain of survival drawn from the community, dispatch center, ambulance and hospital working together. Early cardiopulmonary resuscitation and defibrillation has the greatest impact on survival. If the community response does not restart the heart, resuscitation is continued by emergency medical services staff. There is uncertainty about the best approaches for airway management and the effectiveness of current drug treatments. Prognostic factors and termination of resuscitation rules may guide the duration of a resuscitation attempt and decision to transport to hospital. If return of spontaneous circulation is achieved, the focus of treatment shifts to stabilization, restoring normal physiological parameters and transporting to hospital for on-going care.

Introduction

Out of hospital cardiac arrest (OHCA) is a global health problem, with survival rates varying greatly between communities (1, 2). The chain of survival provides a useful concept to understand differences in pre-hospital emergency care systems that result in such variations in survival (3). Survival of OHCA patients requires a coordinated set of actions including immediate recognition of cardiac arrest and activation of the emergency response system, early cardio-pulmonary resuscitation (CPR), rapid defibrillation, effective advanced life support and integrated post-cardiac arrest care. The chain of survival encompasses the community, emergency medical dispatch, ambulance and hospital based services. Much medical literature has been focused on hospital and advanced life support treatments relative to community and basic life support (BLS) issues (see figure 1). However in recent years, there has been increasing recognition of the importance of BLS, the role of the community, and the key function of emergency medical dispatch in coordinating bystander CPR, early defibrillation and how this impacts survival (4) (5).

Figure 1: Current relative emphasis versus survival impact of elements in the chain of survival



Search strategy and selection criteria

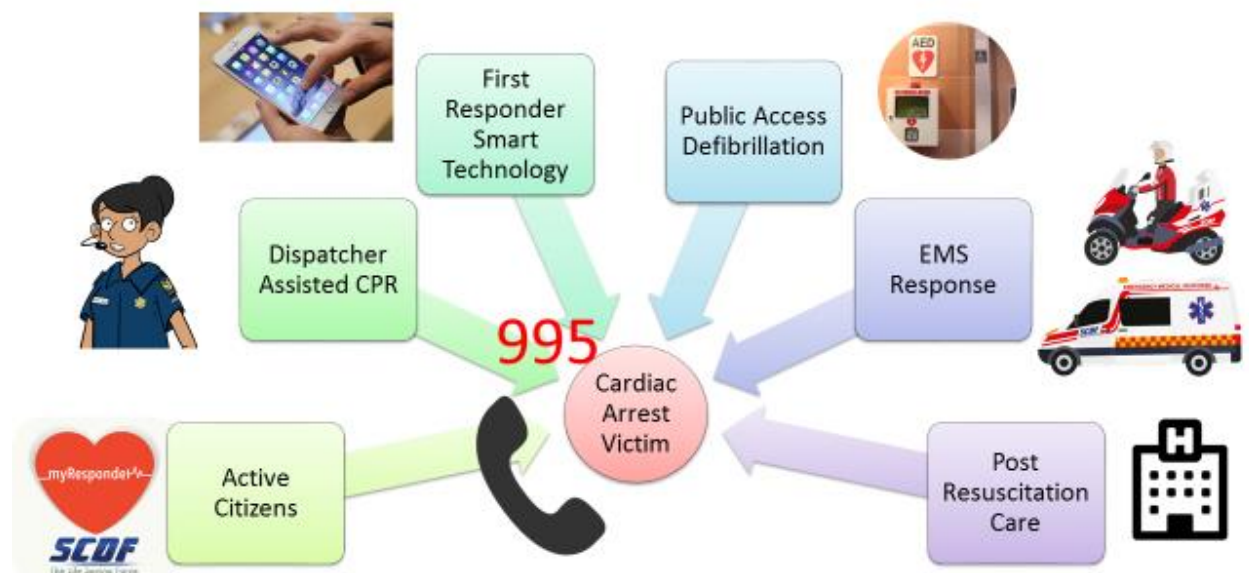
In this expert opinion review, we consider the pre-hospital management of OHCA and important issues in the pre-hospital resuscitation of OHCA victims, with a focus on the first links in the chain-of-survival. We searched the Cochrane Library (2001-2017), MEDLINE (2001-2017), and EMBASE (2001-2017). We used the search terms “cardiac arrest” or “resuscitation” in combination with “dispatch”, “ambulance”, “pre-hospital” emergency medical services”, “defibrillation” or “cardio-pulmonary resuscitation”. We largely selected publications in the last 10 years, but did not exclude commonly referenced older publications. We also searched the reference lists of articles identified by this search strategy and selected those we judged relevant. Our reference list was modified on the basis of comments from peer reviewers

Role of the community working with dispatch The earlier CPR is started, the more likely that chances of survival for OHCA will be improved (6). In an Ontario, Canada study, the OPALS investigators concluded that bystander CPR was the most important modifiable factor for OHCA survival, odds ratio 2.98 (95% confidence interval 2.07 to 4.29)(4). The bystander is the ideal person to start initial resuscitation efforts as the response would be almost immediate upon witnessing an OHCA event. Also, the witness to an OHCA is likely to be a family member or acquaintance of the victim, and thus would be the person most motivated to assist (7).

Conventional strategies to improve bystander CPR rates require a concerted public health effort to educate and train the population to perform CPR. These strategies including making learning CPR mandatory in schools and for obtaining a driver's license for example. In general they are labor intensive and require a long term approach to see positive outcomes. It is also a relatively costly strategy, considering the large number of people that would need to be trained in order to see any improvement in bystander CPR rates (8). Despite large-scale training efforts in communities, reported bystander CPR rates have historically remained relatively low. The reasons for this include difficulty in identifying cardiac arrest, fear of causing harm, emotional distress, and reluctance to perform mouth-to-mouth resuscitation(9).

The dispatch center (also known as the 'control room' or 'call center') plays a central role in the co-ordination of OHCA response (Figure 2). In many ways, it is the 'brain' of Emergency Medical Services (EMS) and determines the subsequent dispatch of resources and response to an OHCA.

Figure 2: Systems approach to improving cardiac arrest survival



*CPR: Cardiopulmonary resuscitation; EMS: Emergency medical services
995: Emergency response number in Singapore*

Dispatcher-assisted CPR (DA-CPR) is an attractive intervention to increase CPR rates and survival (10). When a bystander calls the emergency medical response number (for example, 995 in Singapore) to request for help, this creates an opportunity for early identification of OHCA and provision of bystander CPR(11). The medical dispatcher is thus the true ‘first responder’ at the scene, and can be key to prompt recognition of cardiac arrest and initiation of bystander CPR. This requires proper training of dispatchers to ask the right questions, manage the emotional state of the caller and give clear instructions in the form of dispatcher-assisted CPR instructions. Giving ‘just-in-time education’ over the telephone can provide callers with step-by-step instructions on how to perform CPR.

DA-CPR programs have shown they can nearly double the rate of bystander CPR performed (12). Change in protocols to compression-only CPR DA-CPR have made giving instructions simpler for rescuing adults in sudden cardiac arrest (13). Dispatch-assisted compression-only CPR has been shown to result in less delay in starting CPR, higher participation and better outcomes in early cardiac arrest (14). The experience in Singapore has been that a comprehensive DA-CPR program which included dispatcher training focusing on communication/persuasion, review of audio recordings of all OHCA calls, giving feedback to dispatchers and public education on DA-CPR has resulted in doubling of bystander CPR rates with increase in survival (15).

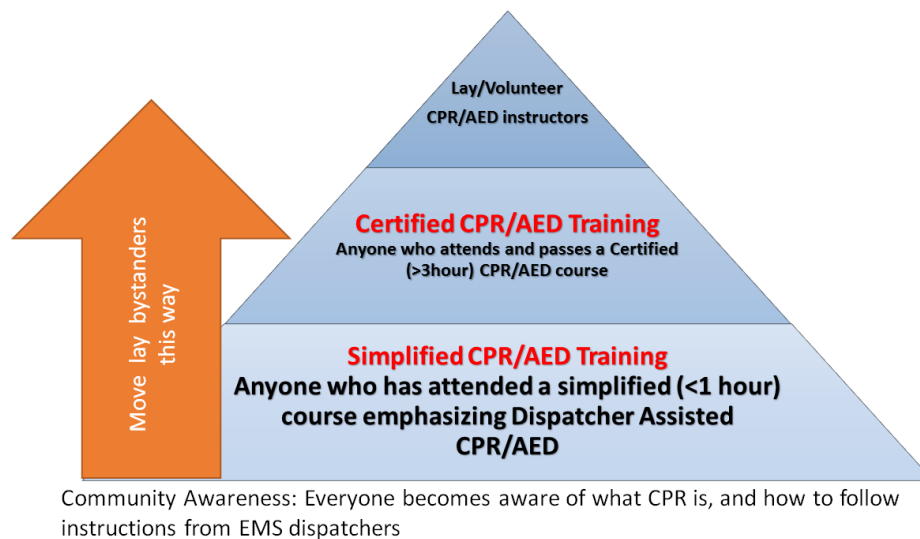
Problems with recognition of cardiac arrest by the public and the dispatcher

One of the main barriers to timely initiation of EMS response and initiation of CPR is difficulty recognizing OHCA by the public, and similarly challenges for dispatchers to diagnose OHCA over the telephone (16). In particular, a patient in cardiac arrest may still have gasping movements, due to agonal breathing that may be misinterpreted as normal respiration(12). This has led to the development of ‘No, No, Go’ protocols by pioneering EMS systems such as Seattle, USA (17) which have been increasingly adopted. These protocols emphasize deliberate initiation of DA-CPR instructions if the response to 2 initial questions is ‘No’: ‘Is the person conscious?’ and ‘Is the person breathing normally?’. Such protocols have been able to dramatically increase the rate of bystander CPR (18). However such protocols also increase the likelihood that a person who is not in cardiac arrest might receive chest compressions, although in practice this has not resulted in any reported adverse outcomes. In the near future, video assisted dispatch technologies might be able to enhance the ability of dispatcher to recognise OHCA.

Public education and community CPR/AED training

There has been increasing understanding that prompt CPR and defibrillation is important for OHCA survival, regardless of who performs it (19). Reducing ambulance response times is challenging for most EMS systems, and may not be a cost-effective policy to improve survival (20). Simplified training programs have shown potential to reach a larger audience and actively recruit lay persons into community efforts. For example a large public campaign focusing on compression only CPR in Arizona was successful in increasing bystander CPR rates as well as survival (21). The aim should not be to dilute the quality of CPR training, but to extend the reach into the community to build a ‘pyramid of responders’ (Figure 3).

Figure 3: Building a pyramid of first responder preparedness*



CPR: Cardiopulmonary resuscitation; AED: Automated external defibrillator

** All training programs referred to include hands on practice and not just exposure to theory*

Public access defibrillation strategies

The key challenge to improve public access defibrillation strategies is how to link willing lay responders to public access defibrillators. Just installing public-access AEDs without an emphasis on linking them to responders may not improve survival. However community wide programs, for example in Japan (19), that integrate public training on CPR with increased access to AEDs, have been able to increase odds of neurologically intact survival.

While cost is still a potential barrier to dissemination of AEDs, strategic placement of AEDs may be a more pressing issue. For example, Folke et al (16) estimated that for the city of Copenhagen, 1104 AEDs would be required to cover 67% of arrests with the cost per quality-adjusted life year (QALY) gained being USD \$40,900 (22). However this cost could possibly be reduced with use of smart technologies to link existing AEDs with lay responders.

Smart technologies for activation of lay responders

One exciting development in recent years has been the potential of smartphone technology to ‘amplify’ the impact of volunteer first responders and public AEDs. Building a national registry of AEDs and making it available to the public is a crucial pre-requisite for success. Ringh et al was able to use mobile-phone positioning to alert volunteers to significantly increased rates of bystander-initiated CPR for OHCAs (23). Smartphone technology can help locate the OHCA victim and the nearest AED. In a world where smartphones become increasingly common, application of this technology could be a potential ‘game changer’. Another interesting possibility in the near future is using AEDs mounted on drones to send to bystanders performing CPR (24).

Decision to resuscitate

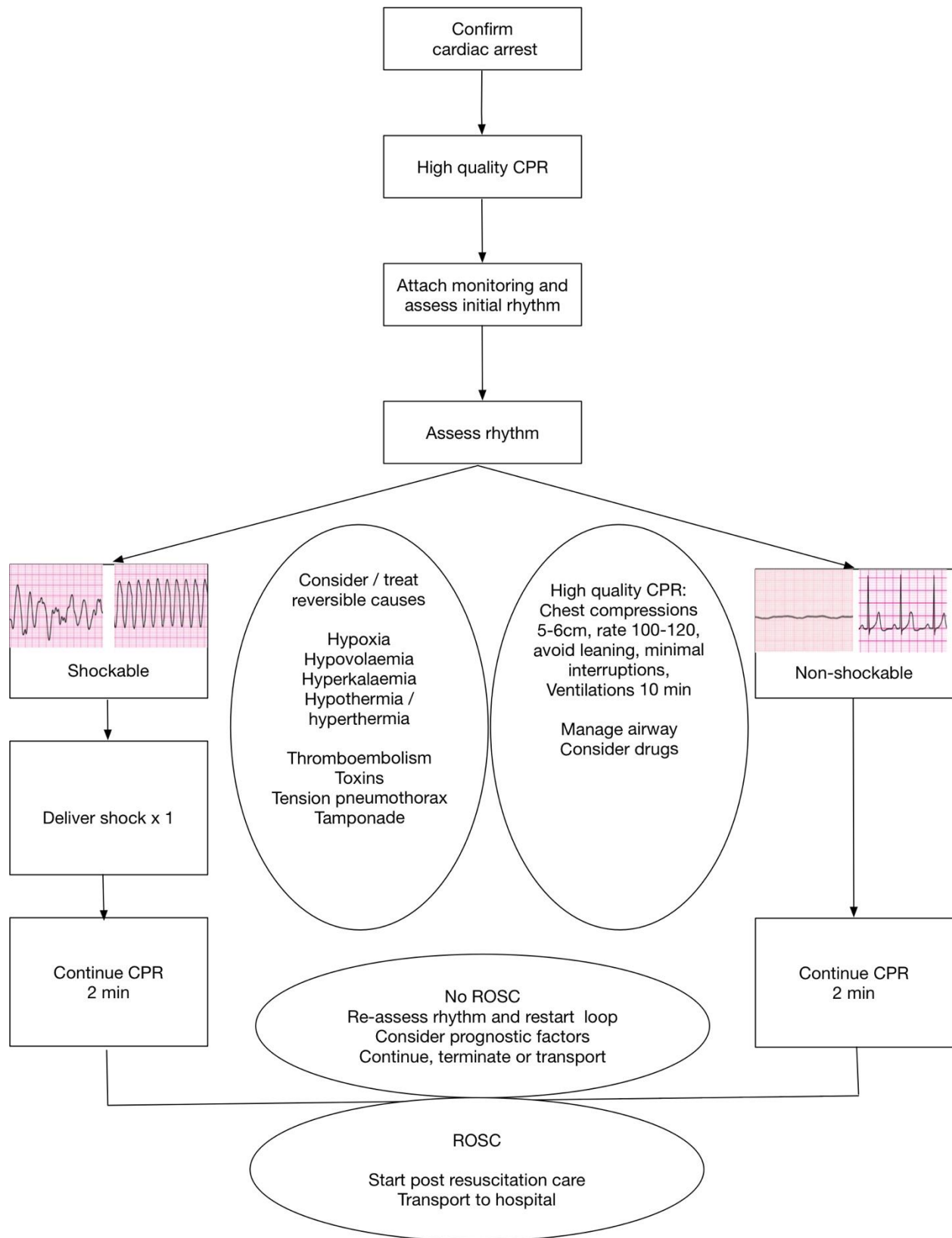
Early descriptions of resuscitation described its application for “hearts that are too good to die” (25). Resuscitation started promptly in such cases has the greatest chance of success. If resuscitation efforts are delayed (as often occurs in an un-witnessed cardiac arrest or when no bystander CPR is provided), the chances of successful resuscitation are substantially reduced. Resuscitation in situations where a patient is reaching the end of their natural life may prolong suffering with little chance of leading to overall benefit.

There are differences in international approaches to the decision to commence or continue resuscitation. In many, but not all settings, resuscitation will be withheld if there is evidence of irreversible death (e.g. rigor mortis, dependent lividity (hypostasis), un-survivable injuries) (26). In some countries, adverse prognostic factors (e.g. un-witnessed cardiac arrest, no bystander CPR for more than 15 minutes, asystolic rhythm and absence of a potentially reversible cause (e.g. hypothermia)) may lead to resuscitation being withheld (27). In other countries resuscitation would be provided in such circumstances (28). In some jurisdictions, advanced decisions to withhold resuscitation may be recorded prior to a cardiac arrest (29, 30).

EMS response and interventions (including Pharmacotherapeutic interventions)

Resuscitation efforts by health care professionals usually follow the generic principles of the Universal Treatment Algorithm (31). After confirming cardiac arrest by identifying the absence of normal breathing (and absence of a central pulse for those experienced in central pulse palpation), chest compressions (5-6cm depth, rate 100-120 min⁻¹, minimal interruptions) are delivered while cardiac monitoring is established (Figure 4) (32). If the initial rhythm is ventricular fibrillation or ventricular tachycardia, defibrillation is attempted followed by immediate resumption of chest compressions. For non-shockable rhythms (pulseless electrical activity and asystole) chest compressions are continued. Prior to securing the airway, chest compressions are paused every 30 compressions to allow the delivery of 2 ventilations (33, 34). Once the airway is secured continuous chest compressions with intermitted ventilations are recommended (34).

Figure 4: Advanced life support treatment algorithm



There is controversy about the optimal approach to airway management in OHCA. Observational studies have produced conflicting results when comparing basic (e.g. bag-valve-mask) with advanced airways (e.g. intubation, supraglottic airways) (35-37). The training and experience of the operator undertaking airway management is likely to be a significant contributing factor (38). The recently completed AIRWAYS 2 and PARC trials will provide valuable information on the optimal approach to airway management in out of hospital cardiac arrest.

Use of drugs has featured in cardiac arrest algorithms since their inception. Two land mark studies found no evidence that drugs improved outcomes. The Ontario Pre-hospital Advanced Life Support (OPALS) study examined outcomes before and after the introduction of advanced resuscitation techniques (intubation and drugs) (39). The study found no evidence of improved survival (5.0% versus 5.1%, $P=0.83$) or favourable neurological outcome (3.9% versus 3.4%, $P=0.73$). Olasveengen *et al* randomized 916 patients to resuscitation with intravenous drugs or without intravenous drugs (40). Patients allocated to the intravenous drug arm had a higher rate of ROSC (OR 1.99, 95% CI, 1.48-2.67) but no difference in survival (OR 1.16, 95% CI 0.74-1.82) or survival with favourable neurological outcome (OR 1.24, 95% CI, 0.77-1.98).

Adrenaline is often given to patients in shockable rhythms which are refractory to attempted defibrillation and to those in non-shockable rhythms. The rationale for administration is that it increases aortic diastolic pressure and improves coronary perfusion. Experimental studies, however, suggest that it may impair cerebral blood flow and increases ventricular arrhythmias and induce myocardial dysfunction after ROSC (41). Early resuscitation algorithms recommended administration of 0.5mg intracardiac or 10mg intravenously (42). Subsequent randomized controlled trials found no benefit to high dose adrenaline leading to the dose being reduced to 1mg every 3-5 minutes (43). Jacobs *et al* compared 1mg adrenaline every 3-5 minutes with placebo in a randomized controlled trial in Australia (44). The trial recruited 601 adults with out of hospital cardiac arrest of any cause, where resuscitation was commenced by paramedics. The trial faced recruitment challenges meaning that when it closed it had only recruited 10% of the intended sample size. The study found evidence of improved return of spontaneous circulation (OR 3.4, 95% CI 2.0 to 5.6) but no difference in long term survival (OR 2.2, 95% CI 0.7 to 6.3). The PARAMEDIC2 trial, which compared 1mg adrenaline every 3-5 minutes with placebo closed to recruitment in October 2017 will provide further information about the safety and effectiveness of adrenaline (45).

The potent vasopressor, vasopressin, has been studied as an alternative or adjunctive treatment to adrenaline for cardiac arrest. Meta-analysis of trials which in total enrolled over 6000 patients found no improvement in outcomes compared to treatment with adrenaline (43, 46), prompting the International Liaison Committee on Resuscitation (ILCOR) to recommend against its routine use in cardiac arrest (47).

Anti-arrhythmic drugs are recommended when initial attempts at defibrillation fail to achieve return of spontaneous circulation. The randomized controlled Amiodarone or Lidocaine or Placebo Study (ALPS) treated 3026 patients with shock refractory OHCA. Although there was no difference in the primary outcome of survival to discharge or favourable neurological outcome in the overall trial population, outcomes were better in those who received drugs if the cardiac arrest was witnessed by a bystander or EMS. For bystander witnessed cardiac arrest, compared to placebo, survival rates were 5% (95% CI, 0.3 to 9.7) higher in the amiodarone group and 5.2% (95% CI 0.5 to 9.9) higher in the lidocaine group. There was no difference between amiodarone and lidocaine (48). The special formulation of amiodarone used in this trial which causes less hypotension, is not widely available which limits the generalizability of this aspect of the study findings.

Manual versus mechanical cardiopulmonary resuscitation

High quality CPR is critical for optimal outcomes from cardiac arrest, yet it is physically demanding and difficult to sustain. Mechanical chest compression devices automate the process and deliver consistent, high quality chest compressions. Two devices have been evaluated in large, multicenter pre-hospital clinical trials which enrolled 12,206 patient with out of hospital cardiac arrest (49). The Autopulse device (Zoll Medical, Chelmsford, MA, USA) consists of a load distributing band which encircles the patients chest and squeezes it against a rigid backboard. The LUCAS device (Physio-Control Inc/ Jolife AB, Lund, Sweden) uses a piston and suction cup to deliver compressions with active recoil. None of the trials individually or when combined in meta-analyses found improved rates of return of spontaneous (OR 0.96, 95% CI 0.85, 1.10), survival at hospital discharge/ 30 days (OR 0.89, 95% CI 0.77, 1.02), or favourable neurological outcome (OR 0.76, 95% CI 0.53, 1.11).(50) These findings led ILCOR to recommend against the routine use of mechanical chest compression devices (47).

Despite the absence of benefit from strategies which routinely deploy mechanical chest compression in out of hospital cardiac arrest, there remain situations where manual chest compressions are either not possible or hazardous where it is reasonable to consider mechanical CPR. Examples include during land ambulance / helicopter transfer to hospital, during percutaneous coronary interventions and as a bridge to advanced therapies (e.g. Extracorporeal-CPR). Mechanical CPR has also been used to maintain organ perfusion when resuscitation has been unsuccessful prior to organ donation. If mechanical CPR is deployed it is important that interruptions to chest compressions are kept to a minimum (< 10-20 seconds). Training resuscitation teams in a pit-stop approach, with a focus on non-technical skills can substantially reduce interruptions to CPR during deployment (51).

Refractory arrest: transport or termination of resuscitation?

There are no absolute rules on the optimal duration of resuscitation. Factors associated with better outcomes (e.g. witnessed arrest, initial shockable rhythm, bystander CPR), presence of potentially reversible causes may guide clinicians to continue with resuscitation efforts for longer. In a recent analysis, the elapsed duration at which the probability of survival fell below 1% was 48 and 15 min in the shockable and non-shockable groups, respectively (52). A secondary analysis of 11,368 cases of OHCA from the US ROC-PRIMED (Resuscitation Outcomes Consortium Prehospital Resuscitation Using an Impedance Valve and Early Versus Delayed) identified that that with conventional resuscitation, 90% of patients with good outcome achieved initial ROSC within 20 minutes and 99% within 37 minutes (53). There were no survivors with favourable neurological outcome where ROSC occurred after 47 minutes. Similar observations were made in a Japanese registry study involving 282,183 bystander witnessed OHCA cases (54).

Over the last decades, it became necessary to provide clinical prediction rules for the termination of resuscitation for avoiding futile transports. Consequently, several teams have developed and prospectively tested unequivocal termination of resuscitation (TOR) rules, which may be applied by prehospital healthcare providers even in the absence of a physician.

When to stop initial resuscitation efforts?

The TOR rules were originally developed to guide basic life support (BLS) prehospital providers in selection of victims in whom continued resuscitation and transport to hospital would be futile (55). Since then, the BLS TOR Guideline has been prospectively and externally validated in a number of studies using both basic and advanced life support providers and is commonly referred to as the “Universal TOR Guideline” (56-58). The Universal BLS TOR Guideline states that resuscitation can be discontinued in the field by prehospital providers if the following three criteria are met: (1) the cardiac arrest was not witnessed by EMS providers; (2) the patient did not obtain a ROSC despite attempted resuscitation; and (3) no shocks were delivered (i.e. not a shockable rhythm) at any time prior to transport. A prospective validation of the Universal BLS TOR Guideline displayed an excellent specificity and positive predictive value for predicting futility, while reducing the transport rate to 46% of attempted resuscitations by EMS (56). In addition to the Universal BLS TOR Guideline, a Universal ALS TOR rule has been developed for use by responders providing ALS. The ALS TOR Guideline adds 2 criteria to the BLS rule: arrest not witnessed by bystander; and no bystander-administered CPR (Table 1). In a large validation study, it has been established that that both rules accurately identified patients with OHCA who were unlikely to benefit from prolonged CPR and transport to the hospital for further attempts at resuscitation (58). Using these rules to guide decisions to stop resuscitative efforts may substantially decrease the rate of futile emergency EMS transports without appreciably worsening the rate of survival. Lastly, when considering abandoning the resuscitation attempt, a factor that may need to be taken into account is the possibility of prolonging CPR and other resuscitative measures to enable organ donation to take place.

Table 1. Basic Life Support and Advanced Life Support Termination-of-Resuscitation Rules

Basic Life Support	Advanced Life Support
Event not witnessed by emergency medical services personnel	Event not witnessed by emergency medical services personnel
No automated external defibrillator used or manual shock applied in out- of-hospital setting	No automated external defibrillator used or manual shock applied in out- of-hospital setting
No return of spontaneous circulation in out-of-hospital setting	No return of spontaneous circulation in out-of-hospital setting
	Arrest not witnessed by bystander
	No bystander-administered cardio- pulmonary resuscitation

When to transport a refractory cardiac arrest?

Extracorporeal CPR (E-CPR) is being used increasingly when conventional resuscitation efforts fail to achieve ROSC with encouraging results (59). There are several ongoing randomized studies that compare ECPR to conventional CPR in order to determine if this is an effective strategy in refractory CA (60). Interestingly, one of these ongoing trials aims to show that the ECPR can be provided on the resuscitation scene, outside the hospital (NCT 02527031) (61).

Whatever the technique employed, the decision to establish E-CPR should be made early (within 10 minutes) and only in patients in whom there is a reasonable chance of neurological recovery (26) using simple criteria:

- Witnessed arrest;
- CPR provided by witness;
- VT/VF as presenting rhythm;
- Presumed reversible cause (e.g., cardiac, toxic, hypothermia);
- No evidence for severe underlying condition;
- Available mechanical CPR device.

Early activation of the process is essential for decreasing the delay to ECPR. Most impressive results of the ECPR strategy have been observed in case series of patients in whom it has been possible to start the mechanical assistance in a median delay of 64 minutes after the OHCA (62).

Optimizing post resuscitation care

Guidelines from European Resuscitation Council (ERC) and European Society of Intensive Care Medicine (ESICM) (Nolan ICM 2015) provide information on how to optimize the management of the post-resuscitation syndrome. The post-resuscitation care should start at the location where ROSC is achieved. The most important pre-hospital points are circulatory, respiratory and

temperature management. In parallel, all efforts should be made to allocate an adequate orientation toward the most adapted receiving center.

Circulation

Shock is very common in the post-resuscitation period, resulting from the combination of a transient myocardial dysfunction and a vasoplegia phenomenon caused by the whole-body ischemia reperfusion (63). Fluids, noradrenaline, with or without dobutamine, are usually the most effective treatments. Infusion of relatively large volumes of fluid is tolerated remarkably well by patients with post-cardiac arrest syndrome. In the most severe patients with a refractory shock, it might be useful to consider the implantation of a mechanical circulatory assistance as recent encouraging results were reported (20). Importantly, finding and treating the cause of the arrest is of major importance for controlling the post-resuscitation shock.

Temperature control

Currently, it is strongly recommended to provide a targeted temperature management (TTM) by maintaining during at least 24 hours a constant, target temperature between 32°C and 36°C (64). The supporting evidence is based on experimental animal data, non-randomised clinical studies and two small randomized trials. Furthermore, this mostly applies to comatose adults after OHCA with an initial shockable rhythm, while the indication is debated in patients with an initial non-shockable rhythm.

Whether it might be useful to start the TTM during transport was mostly examined in several clinical studies in which cold intravenous fluids were administered after ROSC to induce hypothermia (11, 23, 65-67). Although decreasing the mean core temperature on admission and reducing the time to achieve the targeted temperature, this intervention did not prove its benefit and was associated with significantly increased incidence of adverse events (11). Based on this evidence, prehospital cooling using a rapid infusion of large volumes of cold intravenous fluid immediately after ROSC is not recommended.

Ventilation

A vast majority of patients with ROSC will require endotracheal intubation and mechanical ventilation. A particular attention must be paid to ventilator settings. Avoiding hypoxaemia is the main goal, but considering the evidence of harm after myocardial infarction (68) and the possibility of increased neurological injury after cardiac arrest (69, 70), it is recommended to titrate the inspired oxygen concentration to maintain the arterial blood oxygen saturation in the range of 94–98%. Since the level of arterial pressure in CO₂ may influence cerebral blood flow, both hypocapnia and hypercapnia should be avoided by adjusting tidal volumes and respiratory rate. Adjustment of ventilation to achieve normocarbica can be facilitated by monitoring the end-tidal CO₂ during transport.

Triage and orientation

Many resuscitated patients will develop a post-resuscitation disease, requiring ICU admission and life-sustaining therapies. In addition, finding and treating the cause of the arrest is a priority that may be difficult to ensure in all primary care centers. When there is an evidence for a coronary cause, as reflected by ECG pattern and/or prodromes, it is highly recommended to dispatch these patients toward an available cath lab (71). In this population, nearly all clinical data converge in indicating a benefit associated with early coronary reperfusion (72). Since the publication of the pioneering study (73), several studies have shown that immediate cardiac catheter laboratory evaluation, with early percutaneous coronary intervention (PCI) when indicated, is associated with a better outcome, including survival and neurological recovery(74) . In patients with no clinical nor electrical evidence for a coronary cause, the benefit of the early invasive strategy is debated and the answer will probably come from the several ongoing trials (DISCO, EMERGE, COACT, TOMAHAWK) examining this issue. In these patients, early identification of a respiratory or neurological cause would enable transfer of the patient to a specialized ICU for optimal care and may help in prognosis assessment and treatment indications (75). In comatose patients, a careful prognostication process is recommended, which should be based on multimodal evaluation (76). Withdrawing life-sustaining therapy because of perceived poor neurological prognosis (WLST-N) is a common cause of hospital death after OHCA. Although current guidelines recommend against withdrawing life-sustaining therapy before 72 hours, this practice is common and may increase mortality (77).

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Conflict of interest statement

MEHO is currently Scientific Advisor to Global Healthcare SG and TIIM SG, and holds patents related to using Heart Rate Variability and Artificial Intelligence for medical monitoring. He has no direct conflicts relating to sections written by him. GDP received support as a National Institute of Health Research (NIHR) Senior Investigator and has led studies relating to quality of CPR, mechanical CPR and drugs in cardiac arrest funded by NIHR. He has volunteer roles with UK and European Resuscitation Councils and the International Committee for Resuscitation. A Cariou received fees for lectures from Bard and Astra Zeneca. He has no direct conflicts relating to sections written by him

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